

**REMARKS****Interview with Examiner**

A telephonic interview held 1 April 2004 between the Examiner and the undersigned attorney for the Applicant reviewed recent correspondence between the Examiner and the Applicant, and in particular the reason for a lack of response to the Office Action dated 4 September 2003. The Attorney did not receive the mailed Office Action, and indicated that a Power of Attorney was filed in August 2003 giving notice of a change in representation and a new address for correspondence. The Examiner noted there was no indication that a Power of Attorney had been filed, whereupon the Attorney provided by facsimile a copy of the filed papers and a postcard receipt stamped 29 August 2003 received from the U.S. Patent and Trademark Office.

Thus, because the Office Action of 4 September 2003 should have been mailed to a different address for the attention of a different attorney, it was concluded that the Office Action would be remailed, and that the period for response would be reset to begin with the remailing of the Office Action.

**Remarks on the Claims**

Claims 4, 7, 9 and 12-16 have been canceled, and claims 3, 6 and 10 have been amended. Claims 2, 3, 5, 6, 8, 10, and 11 are currently pending in the application.

The amendments simplify the prosecution by focusing on embodiment of claim 3 and re-writing claim 6 to depend from claim 3. The dependence of Claim 10 has been changed as necessitated by the claim amendments. Claims directed to the embodiment of claim 4 have been canceled or amended without prejudice and Applicants reserve the right to pursue that embodiment in a later filed application.

Specific basis for terms used in the amended and new claims are as follows:

Claim	Term/Phrase	Basis
3	microfluidic unit	Page 6, lines 28-31
3	reservoir as an opening in the substrate surface	The structure of a reservoir is shown in cross-section in Figs 1A and 3. Reservoirs are further described at Page 4, lines 22-27 and Page 7, line 17-24.
6	"at least one operational unit comprising at least two reservoirs connected by at least one	Page 3, line 11: "The microfluidic devices will be characterized by having one or more operational units present in the substrate."

	microchannel in the substrate"	Page 3, lines 14-15: "Each unit will have at least one channel and at least two reservoirs..."
6	removal of the limitation of a 'collar inner surface aligned with the inner surface of the opening'	Page 5, lines 12-13: "Alternatively, the collar inner wall may be displaced from the reservoir inner wall..."
6	"collars are covered with a lid"	original Claim 9

No new matter has been added by the amendments. Reconsideration of the application is respectfully requested. A detailed response to the Examiner's rejections and arguments is set forth below.

### Rejections Under 35 U.S.C. 103

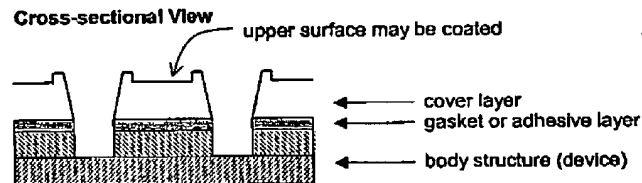
The Examiner has rejected all the pending claims in the application as being unpatentable either over U.S. Pat. No. 5,273,718, issued to Sköld et al., or over Sköld, further in view of U.S. Pat. No. 6,251,343, issued to Dubrow et al. Each claim has been individually addressed in the Examiner's action, with the exception of Claim 16. Applicant assumes that the rejection of Claim 16 would fall within the scope of the argument made against Claims 2-5 and 15.

Sköld describes an apparatus for performing biochemical reactions comprising microtiter plates, a device for receiving and holding the plates and a movably mounted device for applying gas pressure to the wells of the microtiter plate. In Sköld, the microtiter plates have a plurality of wells, with each well having an outlet for fluid expulsion at the bottom. Figure 3 of Sköld illustrates most clearly the essence of the disclosed invention. The planar plate (12) is ringed by two bars (37, 38) housing an inflatable collar (31) which may be brought into contact with the perimeter of the microtiter plate (35) and thereby seal the plenum in place over all the wells of the plate. The space (34) created over the wells may be pressurized for simultaneous processing of all the wells. Note however that the pressurizing gas may not be individually addressed to each of the wells. Also, although the plenum may cap the set of wells, the plenum does not itself constitute a barrier to fluid moving between the wells. The lip present on each well (unlabeled in any figure, and not referred to in the specification) of plate (35) may serve in this regard, however, the lip is in no way contacted by the pressurization device, except maybe for the wells along the perimeter of the plate, and then only partially. The collar (31) indeed seals the plate, but the individual wells are not sealed in the sense that the contents of each well are enclosed and isolated from one another.

Dubrow describes a microfluidic device comprising multiple layers, those layers being determined partly by function and partly by manufacturing concerns. The two main layers are

termed the 'body layer' and the 'cover layer'. Other layers, such as an adhesion layer or a gasket, etc., may be present, as discussed below. The body layer has a plurality of ports, each of which is in fluid communication with channels also in the body. The cover layer has a plurality of apertures through the layer, and which align with the ports in the body layer when the two are mated. A rendering of the disclosed device based on Figure 3B of the patent is shown below:

A cross-sectional view is shown to emphasize the relationship of the cover layer and the body structure. Together, the aperture and the port



combine to form a large well. The cover layer increases the volume capacity of the reservoirs of the body (Col 8, lines 5-10), provides an effective barrier between neighboring reservoirs (Col 7, lines 38-42), and if coated with a hydrophobic material, the coated upper surface helps prevent the deposition or aggregation of fluids on that surface (Col 7, lines 62-66). There is no teaching by Dubrow regarding any lid or cover that might be affixed to the top of the device structure.

Various assertions regarding the teachings in the cited references have been put forth by the Examiner for the different subgroups of claims, and several arguments have been made that are common to more than one subgroup and so for the sake of convenience these will be addressed first collectively and referred to later.

The Examiner in points 4, 6 and 7 of the Detailed Action quotes from Dubrow that "to provide an effective barrier between neighboring reservoirs the upper surface of the cover layer may be coated with a polymer". Continuing in this vein, in the *Response to Arguments* the Examiner finds that, therefore, the cover layer "functions as a cover by preventing cross talk or spillover". Applicant asserts that a cover, in the normal sense and as used in the subject invention, differs in substance from the functional purpose ascribed by the Examiner. The American Heritage Dictionary (4<sup>th</sup> Ed., 2000) defines the noun 'cover' as "something that covers or is laid over or upon something else, as e.g. a lid or a top". In the subject invention, the purpose is in "enclosing, usually reversibly, small reservoirs or other microstructures". (Page 7, lines 28-29). Or, as also stated, the reservoirs are "...sealed on the top side using a film, which seals to the upper surface of the collar". (Page 3, lines 9-10). The cover is also alternatively referred to as a "lid" throughout the application. Applicants assert that the subject invention comprises a lid or cover which

*encloses* the reservoirs of the subject device, and that this functionality is beyond that which is described or taught by Dubrow.

Also, in points 4, 6 and 7 of the Detailed Action it is stated that "The cover layer may be attached to the body structure of the device by adhesive bonding...for tight sealing against evaporation (COL. 9, lines 13-24). Applicants do not find any discussion related to evaporation mitigation with respect to the sealing of the body layer to the cover layer in the cited passage. Referring to the figure on the preceding page, or Fig 3B of Dubrow, it can be appreciated that with regard to the seal between the cover layer and the body layer, leakage or leaching may be an issue, whereas evaporation control would not be a factor. Again, because Dubrow does not mention, suggest or motivate the enclosure of the reservoirs, the Applicants assert that Dubrow does not teach the control or prevention of evaporation in the manner taught by the subject invention, namely that of using a lid to seal the ports of microfluidic devices.

The Examiner rejected claims 2-5 and 15 under 35 U.S.C. 103(a) as being unpatentable over Sköld et al., in view of Dubrow et al., in that Sköld shows a substrate with openings surrounded by a collar, and Dubrow provides the motivation for modifying the apparatus of Sköld to include a conformable lid to provide an effective barrier between reservoirs and better sealing to prevent evaporation. Applicants respectfully disagree with this rejection, particularly in view of the amendments and the above discussion. While Dubrow has taught that appropriate modification of the upper surface may serve as a barrier of sorts between reservoirs (see above), Dubrow does not teach of the need to *prevent* evaporation, nor the means of accomplishing such. Furthermore, should one modify the apparatus of Sköld to include a conformable lid to cover the reservoirs, the apparatus of Sköld would be rendered inoperative. The Sköld apparatus requires the pressurization device to have open access to the wells, and interposing a lid would prevent this. With respect to Claims 3-5 (and 16), Applicants therefore respectfully request that the rejection be withdrawn. Claims 2 and 15, being dependent on the above mentioned independent claims are accordingly asserted to be allowable, and it is respectfully requested that these rejections be withdrawn.

Claim 6 was rejected as being unpatentable over Sköld, in that the volumes of the reservoirs and the dimensions of the collars may be modified appropriately by routine experimentation and thus the claim is not patentably distinct. Applicants respectfully disagree with this rejection, particularly in view of the amendments. Via amendment, Claim 6 now incorporates the limitations of original Claim 7 and 9, among others. Moving to include the arguments directed against Claim 9, the two points discussed above, that a coated upper surface of the cover layer may

be an effective barrier, and that the cover layer may be attached to the body layer by adhesive bonding for tight sealing against evaporation are set forth again by the Examiner. Applicants assert that by the reasoning applied above, these points do not anticipate the subject invention. Further, it would not have been obvious to modify the apparatus of Sköld to include a conformable lid with adhesive coating as an effective barrier between the reservoirs and better sealing between the cover plate and body structure to prevent evaporation. Neither references teaches a lid or cover, nor the need or purpose for such a lid. The adhesive layer of Dubrow is for the binding together of adjacent layers. The effective barrier taught is to prevent the lateral creep of fluid along a surface. The sealing between the cover layer and body layer will not address the control or prevention of evaporation (see above). Lastly, should a conformable lid be applied to the apparatus of Sköld, and specifically to cover the wells of the microtiter plate (35), the apparatus would be rendered inoperative, since the pressurization device would be prevented from communication with the well spaces. Applicants respectfully request that the above rejection be withdrawn.

Claims 7-11 were rejected as being unpatentable over Sköld, in view of Dubrow. Claims 7 and 9 have been canceled, and Claims 8 and 10 now depend from independent Claim 6. Accordingly, it is respectfully requested that the rejections for these claims also be withdrawn, in that they would depend from an allowable claim.

Claims 12-14 were rejected as being unpatentable over Sköld, in view of Dubrow. Pertinent to Claim 12, the Examiner points to the teaching of a flexible gasket by Dubrow, and later asserts that including a lid with a gasket for effective sealing against evaporation would have been obvious. Also, the coated cover layer as an effective barrier, and the tight sealing of the cover layer to the body layer for sealing against evaporation are again recited. In addition to the arguments stated above, Applicants assert that the gasket or the tight sealing of Dubrow is not effective for evaporation control and the limitation of a physical lid enclosing the reservoir is not found in either reference. Furthermore, were one to include such a lid in the apparatus of Sköld, that apparatus would be rendered inoperative, as previously mentioned. Therefore, Applicants respectfully request that this rejection be withdrawn. And, since Claims 13 and 14 depend from Claim 12, the rejections of these claims be withdrawn.

Applicants respectfully traverse the Examiner's arguments that the lid of the subject invention "simply covers the collars". In the specification, it is stated (Page 3, lines 18-23) that: "the sealing cover or lid will be a film, which forms a seal about the collar, so as to at least substantially inhibit fluid flow from the reservoir. The cover will

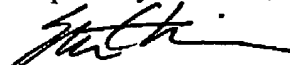
provide for sealing interaction with the collar upper surface, as a result of a compliant surface contacting the collar or an adhesive surface adhering to the upper surface of the collar, particularly an adhesive surface, which is removable.

Thus, Applicants assert that the recitation in the claims of "covered with a lid" (Claims 3, 4 and 6) is, in light of the specification, interpreted as 'sealingly covered with a lid'. The abstract of the application also supports this interpretation: "conformable and/or adhesive lids are employed for sealing the microstructures" (Abstract, lines 9-10). The cover layer of Dubrow is misleading in name because though it may be "an effective barrier" in some manner, it does not literally cover, or, enclose, and thus seal the reservoir, as is claimed herein. The purpose and function of the cover as claimed is neither suggested nor motivated by either reference cited.

Applicants also respectfully assert that, by amendment, a microfluidic device has been claimed in the subject invention. The specification provides a description of microfluidic units on page 3, paragraph 2 and in Figures 2 and 2a and the associated description on pages 6-7. The elements of a device, reservoirs and microchannels are provided on page 4. Claims 3 and 4 recite a microfluidic unit, while Claim 6 recites an operational unit. Please refer to the table above for the basis and meaning of these terms. Thus, Applicants assert that the subject invention as herein claimed is distinguished from the cited prior art and is now in condition for allowance.

For the above reasons, Applicants submit that any basis for the rejections have been overcome by amendment and/or argument and respectfully request that they be withdrawn, and that the claims be allowed and the application quickly passed to issue.

Respectfully submitted,



Stephen C. Macevicz  
Reg. No. 30,285  
Attorney for Applicants

Telephone: (650) 210-1223  
Email: smacevicz@aclara.com